ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

www.surgicalneurologyint.com

Surgical Neurology International

Editor-in-Chief: Nancy E. Epstein, MD, Professor of Clinical Neurosurgery, School of Medicine, State U. of NY at Stony Brook.

SNI: Trauma

Editor
Iype Cherian, MD
Krishna Institute of Medical Sciences; Malkapur, India

SNI
Open Access

Review Article

Neuroprotection: Surgical approaches in traumatic brain injury

Barbara Buccilli[1,2], Albert Alan[2,3,4], Baha' Ghandi Aljeradat[2,5], Akmal Shahzad[2,6], Yasser F. Almealawy[2,7], Nathan Simbarashe Chisvo[2,8], Michelle Ennabe[2,9], Martin Weinand[3,4]

[1]Department of Neurosurgery, Icahn School of Medicine at Mount Sinai, New York City, New York, [2]Global Neurosurgical Alliance, United States, [3]College of Medicine, The University of Arizona College of Medicine - Tucson, [4]Department of Neurosurgery, University of Arizona, Tucson, Arizona, United States, [5]Department of Neurosurgery, The University of Jordan School of Medicine, Amman, Jordan, [6]Department of Medicine, Aga Khan University, Karachi, Pakistan, [7]Department of Neurosurgery, University of Kufa College of Medicine, Kufa, Iraq, [8]Department of Medicine, Barts and the London School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom, [9]College of Medicine, The University of Arizona College of Medicine - Phoenix, Phoenix, Arizona, United States.

E-mail: Barbara Buccilli - doctor.b.buccilli@gmail.com; *Albert Alan - albertalan@arizona.edu; Baha' Ghandi Aljeradat - bjaradat9@gmail.com; Akmal Shahzad - akmal.shahzad@scholar.aku.edu; Yasser F. Almealawy - almealawyyasser@gmail.com; athan Simbarashe Chisvo - nathan_chisvo@outlook.com; Michelle Ennabe - mennabe@arizona.edu; Martin Weinand - mweinand@arizona.edu

***Corresponding author:**
Albert Alan,
Department of Neurosurgery,
University of Arizona, Tucson,
Arizona, United States.

albertalan@arizona.edu

Received: 18 September 2023
Accepted: 05 December 2023
Published: 26 January 2024

DOI
10.25259/SNI_774_2023

Quick Response Code:

ABSTRACT

Background: This review is centered on the pivotal role of surgical interventions within the comprehensive management of traumatic brain injury (TBI). Surgical strategies are indispensable components of TBI care, encompassing primary injury management and the alleviation of secondary injury processes, including the handling of intracranial hemorrhages (ICHs), contusions, and mass lesions.

Methods: A systematic review was carried out by searching databases including PubMed, Embase, and Scopus. The inclusion criteria involved studies discussing surgical strategies for TBI, with a focus on primary injury management, ICHs, contusions, and mass lesions. More recent articles were prioritized, and data were synthesized to assess the impact of surgical interventions on TBI outcomes.

Results: The evolution of surgical technologies has heralded a transformation in TBI management. These advancements encompass minimally invasive procedures, neuroimaging-guided surgeries, and robotic-assisted techniques, all geared toward optimizing patient outcomes.

Conclusion: Surgical interventions within TBI care present unique challenges, such as timing considerations, patient selection criteria, and postoperative care. This review underscores the critical significance of multidisciplinary collaboration among neurosurgeons, neurologists, and critical care specialists. Such collaboration is essential to tailor surgical strategies to the individualized needs of patients. Moreover, the review highlights emerging trends in TBI surgery and underscores the ongoing imperative of research endeavors aimed at refining surgical protocols and ultimately enhancing patient outcomes.

Keywords: Cisternostomy, Decompressive craniectomy, Intracranial hemorrhages, Neuroimaging-guided surgeries, Traumatic brain injury

INTRODUCTION

Background and significance of TBI-related neuroprotection

Traumatic brain injury (TBI) is considered one of the leading causes of morbidity, disability, and mortality across all ages.[22] Unlike other neurological disorders and diseases, TBI is caused by

a mechanical insult, such as a blow or an object penetrating the skull, leading to brain dysfunction. Falls are the most common source of TBI, while other causes include motor vehicle accidents, being struck by an object, and assault.[36]

Any trauma or injury to the brain triggers the activation of a local inflammatory response, primarily mediated by microglia.[38] Damages or injuries to neuronal tissues related to TBI can be classified into two categories: Primary injury, which directly results from mechanical forces during the initial insult, and secondary injury, referring to further tissue and cellular damages following the primary insult.[55]

Primary injury is explained by the displacement of neural tissue and mechanical injury to it, including hemorrhages, vascular damage, contusions, changes in cerebral blood flow (CBF) and blood–brain barrier (BBB) permeability, and metabolic disturbances. Within minutes of the initial mechanical injury, complex biochemical reactions are triggered. These reactions extend for days, months, or even years after the initial injury, causing neuroinflammation, neurodegeneration, and neurological deficits.[31] The therapeutic window for clinical intervention can be extended due to these persisting secondary damage processes [Figure 1].[32,45]

TBI is currently receiving a lot of public attention due to its social and financial costs.[34,72] The prevalence of TBI has increased by 8.4% over the past 26 years, but decades of expensive research have only had a limited impact on clinical outcomes, due to a lack of understanding of the variability and complexity of TBI.[34]

The incidence of TBI varies with age and sex, with males (and especially young men) being more likely to require a TBI-related hospital visit.[23] Globally, the incidence ranges between 100 and 750 cases/100,000 people.[9,25,42,56,59]

The most common kind of TBI identified (70% of cases), mild TBI (mTBI) [Figure 2, Table 1], has a high survival rate, but an estimated 3.17–5 million individuals in the United States now live with chronic impairments related to TBI,[20,23,24] such us motor and cognitive function and social behavior impairments, development of mood disorders, abnormal sleep patterns, and personality changes.[31] Neurodegeneration, dementia, stroke, and epilepsy's risk is significantly increased by severe or repetitive TBI.[80] After an individual sustains an isolated or repeated TBI, there is a potential for hastened neurodegeneration and the development of chronic traumatic encephalopathy. This phenomenon has been observed among athletes and military personnel, particularly those who are exposed to frequent head trauma and experience concussions.[29,48,49]

The direct and immediate brain injury can cause two types of primary brain injury; focal and diffuse injuries.[55] The study showed coexistence of both types of injuries in patients with moderate to severe TBI is common.[67] The hallmark of diffuse TBI is extensive damage of axons predominantly in subcortical, deep white matter tissue, brain stem, and corpus callosum, which involves impairment of axonal transport and degradation of axonal cytoskeleton.[63]

The primary injury often progresses to delayed and prolonged secondary injury. A number of factors contribute to secondary injury: Excitotoxicity, mitochondrial dysfunction, oxidative stress, lipid peroxidation, neuroinflammation, axon degeneration, and apoptotic cell death.[61]

Dysfunction of BBB occurs after 24 h of acute TBI, which allows infiltration of circulating neutrophils, monocytes, and lymphocytes into the injured brain parenchyma.[46]

Scope and objectives of the review

The scope of this review is to comprehensively explore and analyze surgical neuroprotection strategies employed in the context of TBI. Understanding the effectiveness of different interventions is essential to mitigate the impact of TBI and improve patient outcomes. By investigating the available literature and clinical trials, the review seeks to provide a comprehensive overview of the strengths and limitations of each strategy and their potential for translation into clinical practice. Ultimately, the objectives of this review are to inform healthcare practitioners, researchers, and policymakers about evidence-based neuroprotection strategies that hold promise in alleviating the consequences of TBI and fostering better patient recovery and quality of life.

METHODOLOGY

Inclusion and exclusion criteria for article selection

Inclusion and exclusion criteria play a crucial role in ensuring that the articles selected for this review are relevant and meet the objectives of the study. The following are the inclusion and exclusion criteria established for article selection: we included articles that directly address surgical neuroprotection strategies in the context of TBI and that focus on the prevention, reduction, or mitigation of brain injury after a TBI event. Articles published within the past 20 years were given priority to ensure that the review reflects current research and developments in the field. Both preclinical and clinical studies were included. This encompasses animal studies, *in vitro* experiments, as well as randomized controlled trials, cohort studies,case–control studies, and systematic reviews. Only articles written in English were included for ease of comprehension and analysis. Articles that are accessible through academic databases, online journals, and reputable sources were prioritized to ensure reliability and credibility.

Articles not directly related to neuroprotection in the context of TBI were excluded from the study. This includes studies focused solely on other brain disorders or general neurological conditions. Gray literature, conference abstracts,

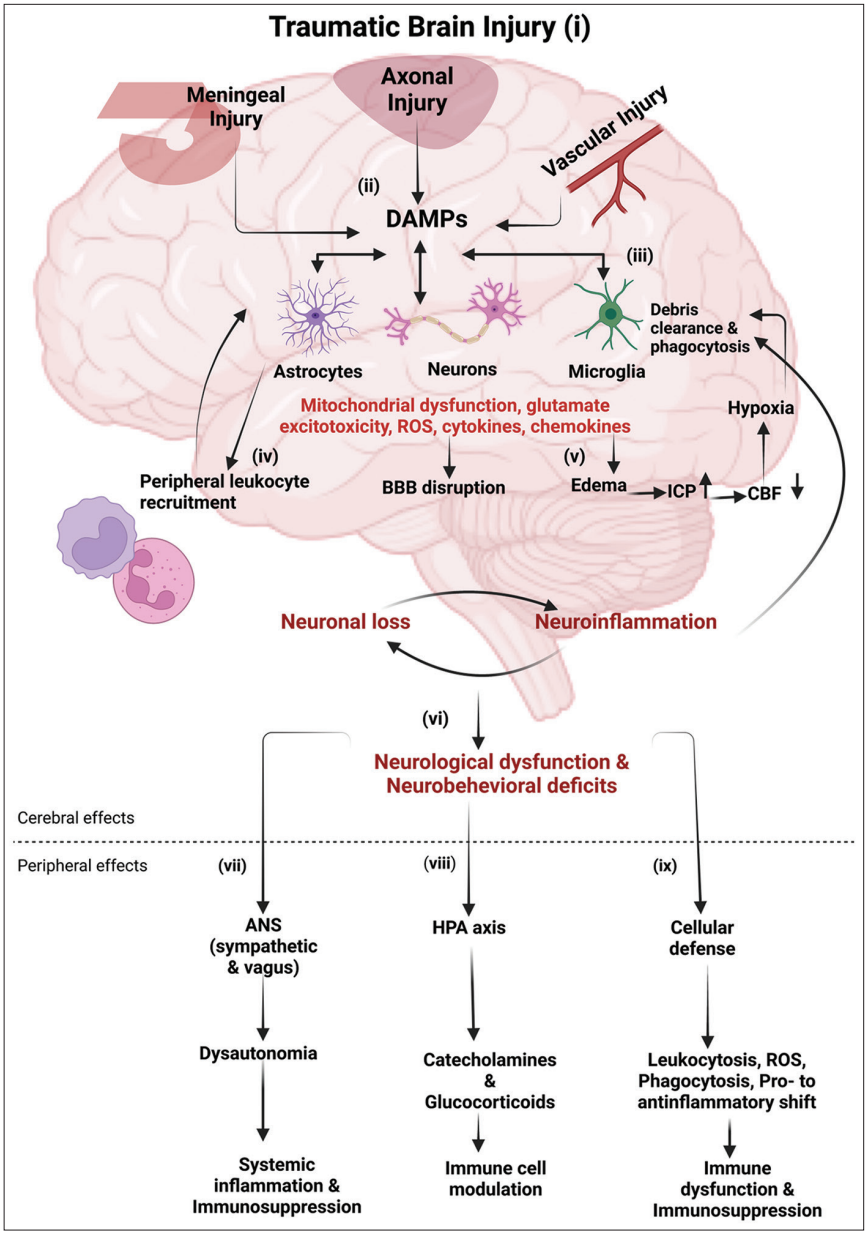

Figure 1: Immune response following traumatic brain injury (TBI): (i-ii) following TBI, the primary mechanical injury can include meningeal contusion, axonal shearing, and cerebrovascular injury, culminating in meningeal and neuronal cell death, as well as microglial and astrocytic activation. (iii) Such neuronal injury and glial engagement generate chemokines, cytokines, and reactive oxygen species, along with the release of damage-associated molecular patterns (DAMPs), setting off an inflammatory response. (iv) In the presence of DAMPs, phagocytic microglia engage in debris clearance and synthesize neurotrophic agents. Sustained stimulation of these pathways induces subsequent injury through leukocyte recruitment, which initially aids in the removal of tissue debris. (v) Subsequently, it contributes to the progression of inflammation and disruption of the blood–brain barrier (BBB). The cytotoxic edema and compromised BBB integrity bring to an elevation of the intracranial pressure, leading to decreased cerebral blood flow, thereby intensifying hypoxia and disrupting the cerebral energy supply. Consequently, this cascade drives further neuronal depletion, propelling a self-perpetuating cycle of neuroinflammation and neurodegeneration. (vi) These progressive pathological modifications culminate in neurological dysfunction and deficits in motor, cognitive, and emotional functions. TBI also induces alterations in the autonomic nervous system (ANS), which monitors and regulates DAMPs, consequently eliciting both cerebral and peripheral immune responses. (vii) Activation of the sympathetic ANS culminates in the peripheral discharge of catecholamines (epinephrine and norepinephrine), which suppress the systemic immune responses of macrophages through the cholinergic anti-inflammatory pathway (CAO), thereby mitigating systemic inflammation. (viii) Furthermore, the release of catecholamines and glucocorticoids through the hypothalamic-pituitary-adrenal axis governs the functional behavior of systemic immune cells after TBI. (ix) The cellular immune response to traumatic brain injury involves an increase in leukocytosis and ROS generation, progresses through phagocytosis, and shifts from pro-inflammatory to anti-inflammatory states, potentially leading to immune dysfunction and immunosuppression. Abbreviations: ICP (increased intracranial pressure), CBF (cerebral blood flow), HPA (hypothalamic-pituitary-adrenal), ROS (reactive oxygen species). Image created with BioRender.com.

editorials, opinions, and non-peer-reviewed articles were excluded due to potential limitations in the rigor and credibility of the information presented. Articles not written in English were excluded, as translation resources may not be readily available and could introduce inaccuracies. In case of duplicate publications, only the most comprehensive and recent versions were included to avoid redundancy.

By adhering to these inclusion and exclusion criteria, the review aims to maintain a high standard of academic rigor, relevance, and reliability. The selected articles will contribute to a comprehensive and evidence-based analysis of surgical neuroprotection strategies in the context of TBI, enabling a meaningful synthesis of findings and implications for clinical practice and future research.

Search strategy and databases used

The following is an outline of the search strategy and the databases used.

We identified relevant keywords and phrases related to the topic, such as "traumatic brain injury," "TBI," "neuroprotection," "neuroprotective agents," "interventions," "clinical trials," and "brain injury outcome." We then combined the identified keywords using Boolean operators (AND, OR) to create effective search strings. For example, (traumatic brain injury OR TBI) AND (neuroprotection OR neuroprotective agents), (neuroprotection OR neuroprotective interventions) AND (brain injury outcome OR clinical trials), (TBI, Neuroprotection, Outcomes evaluation, biomarkers, Imaging techniques, Challenges, "Brain injuries, traumatic"[Mesh], "Neuroprotection"[Mesh], "Outcome assessment, health care"[Mesh], "Biomarkers"[Mesh], and "Diagnostic Imaging"[Mesh]). We included synonyms, alternate spellings, and related terms to capture a broader range of relevant articles.

The databases included in our literature search are PubMed/MEDLINE, Embase, and Scopus. To ensure a thorough search, the reference lists of relevant review articles and included studies will be manually checked for potentially relevant articles that may not have appeared in the initial database search.

By employing this comprehensive search strategy and using reputable databases, the review aims to gather a diverse and extensive collection of literature on neuroprotection strategies in TBI, enabling a robust analysis and synthesis of the available evidence.

SURGICAL APPROACHES

Overview of surgical interventions for TBI neuroprotection

The surgical indications in TBI are broad [Figure 3], and even before considering combined surgical/pharmacological approaches.[4,5,28,64,69] For example, the benefit of transcranial administration of a neuroprotective substance, like antioxidants, is that an elevated local concentration of the medication in the central nervous system can be produced with a little off-target effect in the periphery.[20] Irrespective of the Glasgow coma scale (GCS) score, recent recommendations suggest surgical removal for epidural hematomas (EDHs) exceeding 30 cm^3. In cases of EDH combined with GCS scores below 9, clot thickness surpassing 15 mm, midline shift exceeding 5 mm, or localized neurological impairments, the consideration for surgical evacuation is warranted.[3]

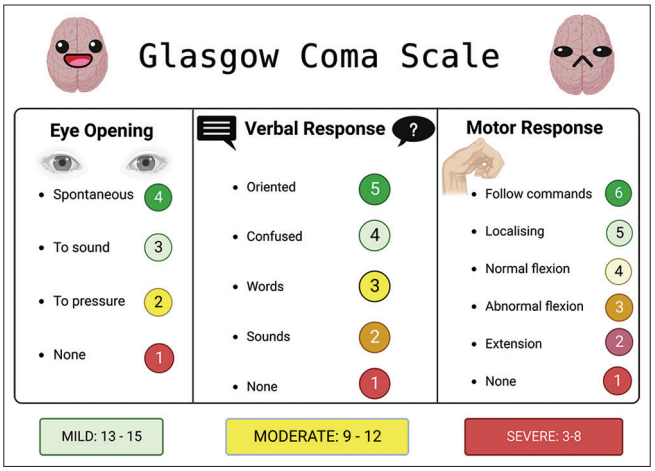

Figure 2: This figure illustrates the Glasgow coma scale (GCS), a vital neurological assessment tool, as it pertains to traumatic brain injury (TBI). The GCS quantifies the patient's level of consciousness based on eye, verbal, and motor responses, aiding clinicians in gauging TBI severity and guiding treatment decisions. Image created with BioRender.com.

Regarding subdural hematomas (SDHs), those exceeding 1 cm, accompanied by midline shifts surpassing 5 mm, a GCS score below 8 with rapid deterioration, or intracranial pressure (ICP) below 20 mm Hg, should all factor into the decision-making process concerning potential evacuation.[6]

Decompression must be taken into account for individuals with parenchymal lesions who have progressive neurologic decline, mass effect, refractory intracranial hemorrhage (ICH), GCS scores of 6–8, frontal or temporal contusions >20 cm^3, midline shift of a minimum of 5 mm, and/or compression of cisterns. This is particularly true if the patients also have lesion volumes >50 cm^3.[5] A considerable reduction in mortality has been observed if evacuation is carried out within four hours following injury.[79]

Decompressive craniectomy (DC) is a procedure that involves removing a significant section of the skull vault to lower ICP and the negative outcomes that it might lead to.[18] The use of 12 15-cm flaps is associated with decreased mortality (26% vs. 35%) and higher extended Glasgow

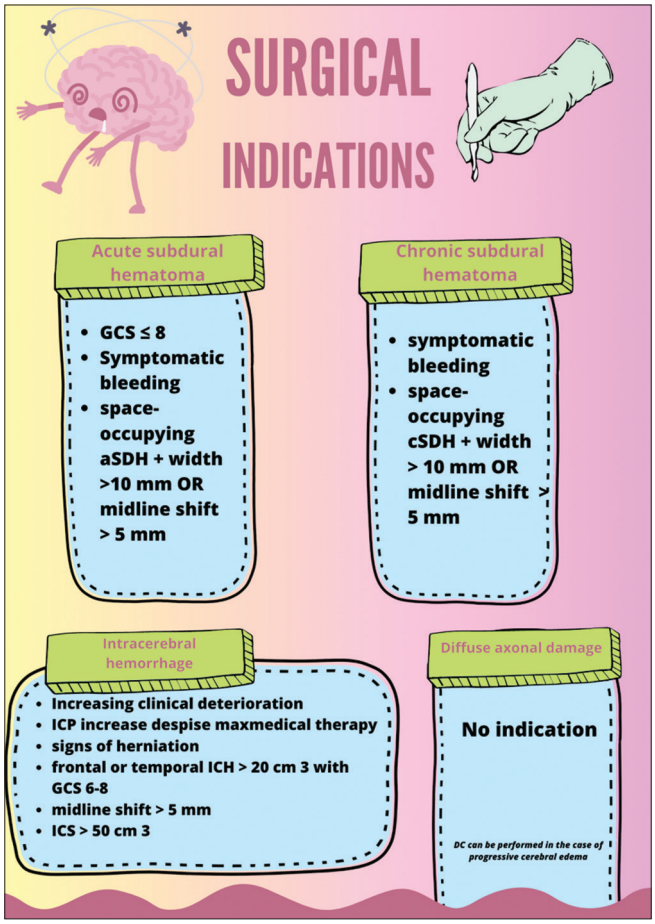

Figure 3: This figure delineates the criteria for surgical intervention across common traumatic brain injury scenarios. Specific clinical and radiological criteria guide the decision to opt for surgery.[4,5,28,64,69] Abbreviations: GCS (Glasgow Coma Scale), cSDH (chronic subdural hematoma), ICS (intracranial suppuration)

outcome scale scores when compared to smaller flap sizes.[35] Primary DC is defined as occurring following the removal of a hematoma in the acute TBI period, and secondary DC as taking place separately from the removal of a hematoma for ICP control.[18,39] In cases with significant herniation risk (i.e., cistern obliteration), bilateral DC may be necessary as a last resort surgical procedure to save the patient with severe bilateral diffuse cerebral edema.[76]

In a patient with considerable concomitant underlying cerebral edema, isolated evacuation of the SDH without interim excision of the bone flap might lead to an additional decline in the patient's conditions following the original operation. Nevertheless, it might be appropriate to perform a craniotomy, with hematoma evacuation and duraplasty, when the underlying brain damage is mild, and the hematoma itself mostly brings on the mass effect.[4]

Acute SDH begins to liquefy after a few days, making less invasive surgical evacuation possible through a bedside

Table 1: Classification of TBI severity based on the GCS score.

TBI severity	GCS score
Mild	13–15
Moderate	9–12
Severe	3–8

GCS: Glasgow coma scale, TBI: Traumatic brain injury

subdural bolt evacuating system. A little cut is made over the SDH, a burr hole is created with a portable twist drill, the dura is opened, and the metal bolt is inserted into the burr hole. The bolt is then secured with a tube that is coupled to a suction mechanism. The main disadvantage is that, when there are many subdural loculations and septations, only the pocket the bolt is covering can be emptied of blood. Surgical intervention may be used to treat a mixed-density SDH that is symptomatic.[71]

In cases of severe TBI, opening cisterns might reduce swelling and the need for decompressive hemicraniectomies through a backshift of cerebrospinal fluid (CSF) through the Virchow-Robin spaces.[12-17] The bidirectional movement of water, facilitating the exchange between CSF and interstitial fluid in the glymphatic system, is primarily mediated by AQP4 channels in response to passive osmotic and hydraulic pressure gradients.[41,58] Consequently, the glymphatic system's functionality is greatly influenced by pressure. This could be behind the "shift edema" in TBI. In terms of patient treatment, cisternostomy has been favored over craniectomy for short- and long-term follow-up [11], and this preference may also be explained by the advantages associated with this procedure.[17] In contrast to decompressive treatments, which may lead to diffuse axonal injury or cortical stretch, cisternostomy improves prognosis, significantly lowering the likelihood of complications and mortality in patients with CSF shift edema.[10,14] It is currently being employed in several neurosurgical departments worldwide.[43]

Evidence from animal models and preclinical studies

Fluid percussion injury (recently updated to a later version, which not only causes localized cortical contusions but also conveys the traumatic damage to subcortical structures, including the thalamus and hippocampi), control cortical impact, weight drop impact acceleration injury, and blast injury model are animal models of TBI which have been regularly employed try to mimic TBI for research purposes.[81]

Animal models of TBI have been used to study the effect of DC on the development of brain edema and subsequent damage following TBI, although the literature is controversial. According to some authors, early craniectomy can prevent later brain injury and markedly decrease cerebral edema accumulation.[73,82] Others, however, obtained

different results.[70] The various outcomes might be related to TBI models' diverse damage severity since the severity of the original damage has a strong correlation with the results of craniectomy.[2] More research is needed to determine which types of TBI are suited for DC and which physiological and pathological pathways are associated with functional results following DC in TBI patients.

Clinical trials and surgical outcomes

The DECRA (DC in Diffuse TBI) study, which provided preventive DC (within 72 h of TBI) in patients with diffuse (on computed tomography [CT]) or severe (on GCS score) TBI, investigated the utility of secondary DC in refractory increased ICP after severe TBI.[19] Mortality at six months was 18% in the medical treatment group and 19% in the surgical group. In terms of disability at six months, "44% of patients in the surgical arm had a favorable outcome, compared to 59% in the control group, while 37% in the surgical group versus 23% in the medical group had an unfavorable outcome." These results suggest that preventive DC does not help patients. DC is also not recommended for mTBI. The POLAR and Eurotherm 3235 studies gave similar results. Based on these findings, the BTF's 2016 guidelines do not suggest bifrontal DC as an approach toward better neurologic outcomes, but they do advocate for a large frontoparietal DC.[7]

A subsequent multinational prospective randomized controlled trial study called randomized evaluation of surgery with craniectomy for uncontrollable elevation of ICP compared medical management alone with medical management together with DC as a treatment for TBI patients who had severe, persistent, and unresponsive intracranial hypertension.[33] Secondary DC led to decreased death rates at six months (26.9% vs. 48.9% in the medical group). About 42.8% of surgical cases and 34.6% of medical patients had favorable outcomes. Surgical patients had "unfavorable" results in 30.4% of the time compared to 16.5% of medical cases.[33] These data show that DC can lower mortality as a last-resort treatment for elevated ICP but at the expense of a greater likelihood of severe impairment and permanent vegetative state.[19,33,40] Due to problems with recruiting, the STITCH (Trauma) study was terminated early, but it demonstrated a mortality reduction in patients who received early operational intervention.[51]

EVALUATING NEUROPROTECTION OUTCOMES

TBI remains a significant public health concern, and the identification of suitable outcome measures which are reliable and reflective of the full picture of the patient's condition is extremely important.

The use of biomarkers in neuroprotection research

Biomarkers have emerged as critical tools in advancing our understanding of neuroprotection after TBI and in optimizing therapeutic approaches. A novel approach introduces that bioactive nanofibrous dural substitutes, fabricated using polycaprolactone nanofibers encapsulated with hyaluronic acid methacryloyl and insulin-like growth factor 1 (IGF-1), offer controlled release of IGF-1.[78] The controlled release mechanism ensures sustained availability of IGF-1, promoting the viability and growth of neural cells post-TBI. This approach not only demonstrates the power of biomaterial engineering but also underscores the significance of biomarkers in optimizing therapeutic interventions.

A recent study pioneers the use of acute treatment with a TrkB agonist to confer neuroprotection and preserve myelin integrity. By leveraging spectral confocal reflectance microscopy, the study unveils the subtle yet crucial changes occurring at the cellular level.[26]

Expanding on this, another project highlights the potential of neuronal CD200 as a biomarker for predicting stroke outcomes and tailoring neuroprotective interventions by diving into the role of neuronal CD200 signaling in the acute phase of ischemic stroke.[1] By knocking out the neuronal CD200 gene, the researchers uncover a pivotal link between CD200 signaling and post-stroke inflammation.

Research also explores the inhibition of high mobility group box 1 (HMGB1) as a strategy to modulate microglia/macrophage polarization after TBI.[27] HMGB1 inhibition has been shown to impact the phenotypic shift of microglia and macrophages, potentially influencing the neuroinflammatory response. This study showcases how targeting specific biomarkers can reshape the immune milieu within the injured brain, offering new avenues for neuroprotection. Other scientists employed several biomarkers to evaluate the effects of the treatment strategy on brain pathology and neuroprotection.[57] The study focused on biomarkers associated with Alzheimer's disease, including amyloid beta peptide and phosphorylated tau, both of which are key players in the pathological process. In addition, the study likely assessed markers of inflammation, oxidative stress, and neuronal damage to understand the broader impact of the treatment.

Another study focuses on the effectiveness of the NADPH oxidase 2 (NOX2) inhibitor GSK2795039 in providing neuroprotection. NOX2 is implicated in oxidative stress, a prominent contributor to TBI pathology.[77] By inhibiting NOX2, GSK2795039 shows promise in mitigating oxidative damage and promoting neuroprotection. This highlights how biomarkers linked to oxidative stress can guide the development of targeted interventions.

A similar study showcases the remarkable potential of gene therapy for neuroprotection.[44] Using ciliary neurotrophic

factor gene therapy, researchers demonstrated lifelong protection against photoreceptor degeneration. This pioneering approach underscores the transformative impact of molecular biomarkers in designing interventions that extend beyond immediate treatment windows.

Collectively, these studies emphasize the pivotal role of biomarkers in neuroprotection research. From utilizing bioactive nanofibrous substitutes to modulating CD200 signaling, inhibiting HMGB1, targeting NOX2, and harnessing gene therapy, biomarkers serve as guiding beacons, illuminating the path toward effective neuroprotection strategies. By unraveling the molecular intricacies of TBI and its aftermath, researchers are poised to revolutionize how we approach and combat traumatic brain injuries.

The use of imaging modalities in neuroprotection research

Neuroprotection research is undergoing a paradigm shift with the integration of advanced imaging modalities. These cutting-edge techniques provide insights into the structural and functional changes that unfold in the brain following TBI.

Recent findings showed how imaging bridges the gap between TBI and Alzheimer's disease.[66] The study unveils the intricate link between the acetylation of tau protein and the pathogenesis of both conditions. Through imaging, researchers discern the patterns of acetylated tau accumulation, elucidating the shared molecular underpinnings of these devastating neurological disorders.

The utilization of advanced imaging techniques for assessing TBI has significant implications for diagnosis, understanding injury mechanisms, and predicting patient outcomes. CT plays a pivotal role in the initial evaluation by swiftly diagnosing brain injuries, identifying fractures, and guiding surgical decisions. While excelling at detecting focal injuries such as extradural and SDHs, CT has limitations in spotting subtle injuries such as traumatic axonal injury (TAI) and entails ionizing radiation exposure. CT-based scoring systems are explored for predicting TBI outcomes and mortality. Magnetic resonance imaging (MRI) emerges as a sensitive tool for detecting diffuse brain injuries, particularly TAI. Various MRI sequences, including fluid-attenuated inversion recovery (FLAIR) and susceptibility-weighted imaging (SWI), enhance TAI detection. Despite the usefulness of CT-based models for predicting major outcomes, MRI holds promise in identifying subtle neurological changes with functional significance. Advanced neuroimaging techniques offer insights into complex facets of TBI. Diffusion-weighted imaging (DWI) captures water movement, indicating constrained or free diffusion. Acute ischemia results in elevated signal intensity on DWI images, while regions with vasogenic edema appear illuminated on apparent diffusion coefficient maps. Diffusion tensor imaging provides insights into tissue damage, particularly in white matter. Standard MRI sequences (T1, T2, FLAIR, and SWI) excel in TBI diagnosis but come with limitations, requiring specialized equipment and lengthier scan times. Physiological imaging techniques shed light on TBI progression. Perfusion CT generates maps of CBF, aiding tissue viability evaluation. Positron emission tomography visualizes brain activities, revealing insights into TBI pathophysiology. Magnetic resonance spectroscopy (MRS) quantifies brain molecules, with changes indicating neuronal loss or metabolic dysfunction. Proton MRS predicts unfavorable outcomes, especially in specific brain regions. Phosphorous MRS offers insights into cerebral metabolic function. Chronic TBI analysis using advanced imaging methods uncovers reductions in brain volume in regions like the hippocampus. Resting and task-oriented functional MRI (fMRI) elucidate network changes and adaptation, highlighting cognitive deficits and reorganization. fMRI even challenges prior assumptions about patient responsiveness, reshaping recovery assessment post-brain injury.[8]

CHALLENGES

Neuroprotection research for TBI stands at the crossroads of scientific discovery and clinical translation, yet navigating this complex terrain is rife with challenges. Research sheds light on the intricacies of clinical trials focused on neuroprotective interventions.[53] The nuanced interplay between treatment efficacy, patient selection, and trial design is analyzed through the lens of failed progesterone trials. There are formidable challenges inherent in conducting large-scale clinical trials, where the unpredictable nature of TBI outcomes poses a formidable hurdle.

In the realm of age-related variations, a recent work confronts the complex challenge of translating neuroprotective interventions across different age groups.[30] The intricate interplay between age, injury severity, and molecular response complicates the development of universal therapies. This study emphasizes the necessity of tailoring interventions to address the unique needs of diverse patient populations, heralding a personalized approach to neuroprotection.

The longitudinal aspect of neurodegenerative diseases takes center stage, particularly when dealing with the intricacies of investigating gradual-progressing conditions. This becomes especially pertinent in the context of gene therapy for neuroprotection, where the necessity for enduring evaluations becomes evident. The formidable challenge of ensuring continuous interventions and evaluations over extended periods is highlighted, thus unveiling the intricate

process of converting promising research into concrete clinical outcomes.[44]

CLINICAL IMPLICATIONS

Translating neuroprotection strategies to clinical practice

Enhancing TBI care requires an important transition from experimental neuroprotection techniques to practical applications in clinical settings. To enable the smooth incorporation of these strategies into standard clinical protocols, this phase necessitates precise planning and thorough review. The implementation of neuroprotection strategies calls for the creation of standardized guidelines and protocols that complement current therapeutic modalities. Validating the safety, effectiveness, and practicability of these therapies calls for extensive clinical trials and real-world investigations to bridge the gap between laboratory research and clinical realities. Neurologists, neurosurgeons, rehabilitation experts, and other medical professionals must work well together and communicate well to develop a coordinated strategy that maximizes patient care while maximizing the potential advantages of neuroprotection techniques.

Challenges in implementation and personalized approaches

Despite the great potential of neuroprotection techniques, their effective application faces several difficulties. Variability in the patient's characteristics, the severity of the injury, and the patient's reaction to therapy emphasize the need for individualized strategies suited to each TBI case. Getting over logistical problems, gathering funds, and educating healthcare professionals are necessary for integrating neuroprotection techniques into a wide range of clinical settings. Adoption of novel interventions necessitates a difficult balancing act between the need for quick deployment of efficient therapies and the comprehensive assessment necessary for their safe and successful application. The creation of flexible and scalable procedures that take into account the intricate interaction of clinical, logistical, and patient-related elements is essential for overcoming these obstacles.

ICP and CPP offer insights into CBF dynamics. Yet, metabolic events can be assessed through probes, like $PbtO_2$, reflecting extracellular oxygen tension.[37,47,75] $PbtO_2$'s balance of oxygen delivery, consumption, and metabolic rate is influenced by oxygen diffusion.[52,62] Diffusion challenges arise in regions like pericontusional tissue due to edema and microvascular collapse, reducing oxygen tension.[52] Defining optimal $PbtO_2$ target values is complex; oxygen tensions near 23 mm Hg occur during functional neurosurgery.[60] Levels between 15 mm Hg and 20 mm Hg signal insufficient oxygen supply, linked to poor TBI outcomes.[52,65,74] Strategies to restore $PbtO_2$ involve manipulating arterial pressure, oxygen tension, or both.[50,68] These approaches show promise for better outcomes than those focusing solely on ICP and CPP. However, limited controlled trials weaken the evidence.[54]

Although the prospect of using enhanced multimodal monitoring to direct care in older patients is enticing, there is little concrete knowledge in this area. This lack of insight can be partially explained by the higher risks associated with invasive intracranial monitoring in older patients, who frequently present taking anticoagulant and antiplatelet medications, in part by the likelihood of a suboptimal outcome, which has led to a lowered frequency of aggressive monitoring and therapy in this population.

DC was performed for the management of unilateral or bilateral brain swelling in TBI patients older than 66 years; unfortunately, in this study, mortality was 77%, and overall unfavorable outcomes occurred in 82%, so this strategy has been discontinued in clinical practice for patients over the age of 65 who present with a GCS of 8 or less.[21]

Ethical considerations and patient perspectives

In the context of surgical approaches, ethical considerations and the viewpoints of patients are critical factors that significantly influence clinical decisions and treatment strategies. These elements underscore the importance of respecting the autonomy and preferences of patients while ensuring that medical interventions are guided by ethical principles such as beneficence and justice. Furthermore, dealing with intricate ethical dilemmas related to issues such as the appropriateness of medical interventions, allocation of resources, and the influence of cultural beliefs necessitates a careful and patient-centric approach. By involving patients and their families in shared decision-making, offering comprehensive information, and advocating for their needs, healthcare providers can effectively navigate these ethical complexities and enhance patient outcomes.

CONCLUSION

TBI remains a significant public health concern, and researchers have tirelessly explored diverse therapeutic approaches to mitigate its debilitating consequences. The diverse range of neuroprotective strategies underscores the complexity of TBI management. Even if neurosurgery plays a pivotal role in TBI management, no single intervention appears to provide a panacea for this multifaceted condition. Instead, a holistic approach that considers patient-specific factors, timing, and a combination of therapies may hold the key to improving outcomes. Furthermore, ongoing efforts to standardize protocols and refine patient selection criteria will contribute to more reliable outcomes in future treatments.

Ethical approval

Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

REFERENCES

1. Al Mamun A, Ngwa C, Qi S, Honarpisheh P, Datar S, Sharmeen R, *et al.* Neuronal CD200 signaling is protective in the acute phase of ischemic stroke. Stroke 2021;52:3362-73.
2. Bohman LE, Schuster JM. Decompressive craniectomy for management of traumatic brain injury: An update. Curr Neurol Neurosci Rep 2013;13:392.
3. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW, *et al.* Surgical management of acute epidural hematomas. Neurosurgery 2006;58:S7-15.
4. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW, *et al.* Surgical management of acute subdural hematomas. Neurosurgery 2006;58:S16-24; discussion Si-iv.
5. Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW, *et al.* Surgical management of traumatic parenchymal lesions. Neurosurgery 2006;58:S2-46.
6. Cameron JL, Cameron AM. The management of traumatic brain injury. In: Current surgical therapy. 12th ed. Netherlands: Elsevier; 2017.
7. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, *et al.* Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery 2017;80:6-15.
8. Carter E, Coles JP. Imaging in the diagnosis and prognosis of traumatic brain injury. Expert Opin Med Diagn 2012;6:541-54.
9. Cassidy JD, Carroll LJ, Peloso PM, Borg J, von Holst H, Holm L, *et al.* Incidence, risk factors and prevention of mild traumatic brain injury: Results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med 2004;43 Suppl:28-60.
10. Chandra VV, Mowliswara Prasad BC, Banavath HN, Chandrasekhar Reddy K. Cisternostomy versus decompressive craniectomy for the management of traumatic brain injury: A randomized controlled trial. World Neurosurg 2022;162:e58-64.
11. Cherian I, Beltran M, Landi A, Alafaci C, Torregrossa F, Grasso G. Introducing the concept of "CSF-shift edema" in traumatic brain injury. J Neurosci Res 2018;96:744-52.
12. Cherian I, Beltran M. A unified physical theory for CSF circulation, cooling and cleaning of the brain, sleep, and head injuries in degenerative cognitive disorders. Berlin: Springer International Publishing; 2017. p. 773-83.
13. Cherian I, Bernardo A, Grasso G. Cisternostomy for traumatic brain injury: Pathophysiologic mechanisms and surgical technical notes. World Neurosurg 2016;89:51-7.
14. Cherian I, Burhan H. Outcomes of severe head injury patients undergoing cisternostomy at tertiary care hospital in Nepal. Indones J Neurosurg 2019;2:55-9.
15. Cherian I, Grasso G, Bernardo A, Munakomi S. Anatomy and physiology of cisternostomy. Chin J Traumatol 2016;19:7-10.
16. Cherian I, Munakomi S. Surgical technique for cisternostomy: A review. Int J Stud Res 2013;3:5.
17. Cherian I, Yi G, Munakomi S. Cisternostomy: Replacing the age old decompressive hemicraniectomy? Asian J Neurosurg 2013;8:132-8.
18. Cooper DJ, Nichol AD, Bailey M, Bernard S, Cameron PA, Pili-Floury S, *et al.* Effect of early sustained prophylactic hypothermia on neurologic outcomes among patients with severe traumatic brain injury. JAMA 2018;320:2211.
19. Cooper DJ, Rosenfeld JV, Murray L, Arabi YM, Davies AR, D'Urso P, *et al.* Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med 2011;364:1493-502.
20. Corps KN, Roth TL, McGavern DB. Inflammation and neuroprotection in traumatic brain injury. JAMA Neurol 2015;72:355-62.
21. De Bonis P, Pompucci A, Mangiola A, Paternoster G, Festa R, Nucci CG, *et al.* Decompressive craniectomy for elderly patients with traumatic brain injury: It's probably not worth the while. J Neurotrauma 2011;28:2043-8.
22. Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, Punchak M, *et al.* Estimating the global incidence of traumatic brain injury. J Neurosurg 2019;130:1080-97.
23. Faul M, Coronado V. Epidemiology of traumatic brain injury. Handb Clin Neurol 2015;127:3-13.
24. Faul M, Wald MM, Xu L, Coronado VG. Traumatic brain injury in the United States; Emergency department visits, hospitalizations, and deaths, 2002–2006. US: National Center for Injury Prevention and Control; 2010.
25. Feigin VL, Theadom A, Barker-Collo S, Starkey NJ, McPherson K, Kahan M, *et al.* Incidence of traumatic brain injury in New Zealand: A population-based study. Lancet Neurol 2013;12:53-64.
26. Fletcher JL, Dill LK, Wood RJ, Wang S, Robertson K, Murray SS, *et al.* Acute treatment with TrkB agonist LM22A-4 confers neuroprotection and preserves myelin integrity in a mouse model of pediatric traumatic brain injury. Exp Neurol 2021;339:113652.
27. Gao T, Chen Z, Chen H, Yuan H, Wang Y, Peng X, *et al.* Inhibition of HMGB1 mediates neuroprotection of traumatic brain injury by modulating the microglia/macrophage polarization. Biochem Biophys Res Commun 2018;497:430-6.

28. Gean AD, Fischbein NJ. Head trauma. Neuroimaging Clin N Am 2010;20:527-56.
29. Goldstein LE, Fisher AM, Tagge CA, Zhang XL, Velisek L, Sullivan JA, *et al.* Chronic traumatic encephalopathy in blast-exposed military veterans and a blast neurotrauma mouse model. Sci Transl Med 2012;4:134ra60.
30. Gupte R, Christian S, Keselman P, Habiger J, Brooks WM, Harris JL. Evaluation of taurine neuroprotection in aged rats with traumatic brain injury. Brain Imaging Behav 2019;13:461-71.
31. Hanscom M, Loane DJ, Shea-Donohue T. Brain-gut axis dysfunction in the pathogenesis of traumatic brain injury. J Clin Invest 2021;131:e143777.
32. Henry RJ, Ritzel RM, Barrett JP, Doran SJ, Jiao Y, Leach JB, *et al.* Microglial depletion with CSF1R inhibitor during chronic phase of experimental traumatic brain injury reduces neurodegeneration and neurological deficits. J Neurosci 2020;40:2960-74.
33. Hutchinson PJ, Kolias AG, Timofeev IS, Corteen EA, Czosnyka M, Timothy J, *et al.* Trial of decompressive craniectomy for traumatic intracranial hypertension. N Engl J Med 2016;375:1119-30.
34. James SL, Theadom A, Ellenbogen RG, Bannick MS, Mountjoy-Venning WC, Lucchesi LR, *et al*. Global, regional, and national burden of traumatic brain injury and spinal cord injury, 1990–2016: A systematic analysis for the Global Burden of Disease Study 2016. Lancet Neurol 2019;18:56-87.
35. Jiang JY, Xu W, Li WP, Xu WH, Zhang J, Bao YH, *et al.* Efficacy of standard trauma craniectomy for refractory intracranial hypertension with severe traumatic brain Injury: A multicenter, prospective, randomized controlled study. J Neurotrauma 2005;22:623-8.
36. Keating CE, Cullen DK. Mechanosensation in traumatic brain injury. Neurobiol Dis 2021;148:105210.
37. Kiening KL, Unterberg AW, Bardt TF, Schneider GH, Lanksch WR. Monitoring of cerebral oxygenation in patients with severe head injuries: Brain tissue PO2 versus jugular vein oxygen saturation. J Neurosurg 1996;85:751-7.
38. Kim CC, Nakamura MC, Hsieh CL. Brain trauma elicits non-canonical macrophage activation states. J Neuroinflammation 2016;13:117.
39. Kolias AG, Kirkpatrick PJ, Hutchinson PJ. Decompressive craniectomy: Past, present and future. Nat Rev Neurol 2013;9:405-15.
40. Kolias AG, Viaroli E, Rubiano AM, Adams H, Khan T, Gupta D, *et al.* The current status of decompressive craniectomy in traumatic brain injury. Curr Trauma Rep 2018;4:326-32.
41. Kress BT, Iliff JJ, Xia M, Wang M, Wei HS, Zeppenfeld D, *et al.* Impairment of paravascular clearance pathways in the aging brain. Ann Neurol 2014;76:845-61.
42. Leibson CL, Brown AW, Ransom JE, Diehl NN, Perkins PK, Mandrekar J, *et al.* Incidence of traumatic brain injury across the full disease spectrum. Epidemiology 2011;22:836-44.
43. Levi V, Vetrano IG. May cisternostomy and glymphatic system be considered the deus ex machina of refractory posttraumatic intracranial hypertension? World Neurosurg 2018;117:471-2.
44. Lipinski DM, Barnard AR, Singh MS, Martin C, Lee EJ, Davies WI, *et al.* CNTF gene therapy confers lifelong neuroprotection in a mouse model of human retinitis pigmentosa. Mol Ther 2015;23:1308-19.
45. Loane DJ, Faden AI. Neuroprotection for traumatic brain injury: Translational challenges and emerging therapeutic strategies. Trends Pharmacol Sci 2010;31:596-604.
46. Lotocki G, de Rivero Vaccari JP, Perez ER, Sanchez-Molano J, Furones-Alonso O, Bramlett HM, *et al.* Alterations in blood-brain barrier permeability to large and small molecules and leukocyte accumulation after traumatic brain injury: Effects of post-traumatic hypothermia. J Neurotrauma 2009;26:1123-34.
47. Maas AI, Fleckenstein W, de Jong DA, van Santbrink H. Monitoring cerebral oxygenation: Experimental studies and preliminary clinical results of continuous monitoring of cerebrospinal fluid and brain tissue oxygen tension. Acta Neurochir Suppl (Wien) 1993;59:50-7.
48. McKee AC, Cantu RC, Nowinski CJ, Hedley-Whyte ET, Gavett BE, Budson AE, *et al.* Chronic traumatic encephalopathy in athletes: Progressive tauopathy after repetitive head injury. J Neuropathol Exp Neurol 2009;68:709-35.
49. McKee AC, Stern RA, Nowinski CJ, Stein TD, Alvarez VE, Daneshvar DH, *et al.* The spectrum of disease in chronic traumatic encephalopathy. Brain 2013;136:43-64.
50. Meixensberger J, Jaeger M, Väth A, Dings J, Kunze E, Roosen K. Brain tissue oxygen guided treatment supplementing ICP/CPP therapy after traumatic brain injury. J Neurol Neurosurg Psychiatry 2003;74:760-4.
51. Mendelow AD, Gregson BA, Rowan EN, Francis R, McColl E, McNamee P, *et al.* Early surgery versus initial conservative treatment in patients with traumatic intracerebral hemorrhage (STITCH[Trauma]): The first randomized trial. J Neurotrauma 2015;32:1312-23.
52. Menon DK, Coles JP, Gupta AK, Fryer TD, Smielewski P, Chatfield DA, *et al.* Diffusion limited oxygen delivery following head injury. Crit Care Med 2004;32:1384-90.
53. Meyfroidt G, Taccone FS. Another failed attempt of neuroprotection: Progesterone for moderate and severe traumatic brain injury. Minerva Anestesiol 2016;82:486-91.
54. Nangunoori R, Maloney-Wilensky E, Stiefel M, Park S, Andrew Kofke W, Levine JM, *et al.* Brain tissue oxygen-based therapy and outcome after severe traumatic brain injury: A systematic literature review. Neurocrit Care 2012;17:131-8.
55. Ng SY, Lee AY. Traumatic brain injuries: Pathophysiology and potential therapeutic targets. Front Cell Neurosci 2019;13:528.
56. Nguyen R, Fiest KM, McChesney J, Kwon CS, Jette N, Frolkis AD, *et al.* The international incidence of traumatic brain injury: A systematic review and meta-analysis. Can J Neurol Sci 2016;43:774-85.
57. Nozari A, Sharma A, Wang Z, Feng L, Muresanu DF, Tian ZR, *et al.* Co-administration of nanowired oxiracetam and neprilysin with monoclonal antibodies to amyloid beta peptide and p-tau thwarted exacerbation of brain pathology in concussive head injury at hot environment. Adv Neurobiol 2023;32:271-313.
58. Papadopoulos MC, Verkman AS. Aquaporin water channels in the nervous system. Nat Rev Neurosci 2013;14:265-77.
59. Peeters W, van den Brande R, Polinder S, Brazinova A, Steyerberg EW, Lingsma HF, *et al.* Epidemiology of traumatic brain injury in Europe. Acta Neurochir (Wien) 2015;157:1683-96.
60. Pennings FA, Schuurman PR, van den Munckhof P, Bouma GJ. Brain tissue oxygen pressure monitoring in awake patients

during functional neurosurgery: The assessment of normal values. J Neurotrauma 2008;25:1173-7.
61. Ray SK, Dixon CE, Banik NL. Molecular mechanisms in the pathogenesis of traumatic brain injury. Histol Histopathol 2002;17:1137-52.
62. Rosenthal G, Hemphill JC 3rd, Sorani M, Martin C, Morabito D, Obrist WD, *et al.* Brain tissue oxygen tension is more indicative of oxygen diffusion than oxygen delivery and metabolism in patients with traumatic brain injury. Crit Care Med 2008;36:1917-24.
63. Saatman KE, Duhaime AC, Bullock R, Maas AI, Valadka A, Manley GT, *et al.* Classification of traumatic brain injury for targeted therapies. J Neurotrauma 2008;25:719-38.
64. Samandouras G. Traumatic brain injury. In: The neurosurgeon's handbook. Oxford: Oxford University Press; 2010. p. 207-38.
65. Sarrafzadeh AS, Kiening KL, Bardt TF, Schneider GH, Unterberg AW, Lanksch WR. Cerebral oxygenation in contusioned vs. Nonlesioned brain tissue: Moniting of PtiO2 with licox and paratrend. In: Intracranial pressure and neuromonitoring in brain injury. Berlin: Springer Vienna; 1998. p. 186-9.
66. Singh SP, Jadhav SH, Chaturvedi CP, Nityanand S. Therapeutic efficacy of multipotent adult progenitor cells versus mesenchymal stem cells in experimental autoimmune encephalomyelitis. Regen Med 2017;12:377-96.
67. Skandsen T, Kvistad KA, Solheim O, Strand IH, Folvik M, Vik A. Prevalence and impact of diffuse axonal injury in patients with moderate and severe head injury: A cohort study of early magnetic resonance imaging findings and 1-year outcome. J Neurosurg 2010;113:556-63.
68. Spiotta AM, Stiefel MF, Gracias VH, Garuffe AM, Kofke WA, Maloney-Wilensky E, *et al.* Brain tissue oxygen-directed management and outcome in patients with severe traumatic brain injury. J Neurosurg 2010;113:571-80.
69. Stiell IG, Wells GA, Vandemheen K, Clement C, Lesiuk H, Laupacis A, *et al.* The Canadian CT head rule for patients with minor head injury. Lancet 2001;357:1391-6.
70. Szczygielski J, Mautes AE, Müller A, Sippl C, Glameanu C, Schwerdtfeger K, *et al.* Decompressive craniectomy increases brain lesion volume and exacerbates functional impairment in closed head injury in mice. J Neurotrauma 2016;33:122-31.
71. Tanaka Y, Ohno K. Chronic subdural hematoma - an up-to-date concept. J Med Dent Sci 2013;60:55-61.
72. Te Ao B, Brown P, Tobias M, Ameratunga S, Barker-Collo S, Theadom A, *et al.* Cost of traumatic brain injury in New Zealand: Evidence from a population-based study. Neurology 2014;83:1645-52.
73. Tomura S, Nawashiro H, Otani N, Uozumi Y, Toyooka T, Ohsumi A, *et al.* Effect of decompressive craniectomy on aquaporin-4 expression after lateral fluid percussion injury in rats. J Neurotrauma 2011;28:237-43.
74. Valadka AB, Gopinath SP, Contant CF, Uzura M, Robertson CS. Relationship of brain tissue PO2 to outcome after severe head injury. Crit Care Med 1998;26:1576-81.
75. Van Santbrink H, Maas AI, Avezaat CJ. Continuous monitoring of partial pressure of brain tissue oxygen in patients with severe head injury. Neurosurgery 1996;38:21-31.
76. Walcott BP, Nahed BV, Sheth SA, Yanamadala V, Caracci JR, Asaad WF. Bilateral hemicraniectomy in non-penetrating traumatic brain injury. J Neurotrauma 2012;29:1879-85.
77. Wang M, Luo L. An effective NADPH oxidase 2 inhibitor provides neuroprotection and improves functional outcomes in animal model of traumatic brain injury. Neurochem Res 2020;45:1097-106.
78. Wang Y, Guo Q, Wang W, Wang Y, Fang K, Wan Q, *et al.* Potential use of bioactive nanofibrous dural substitutes with controlled release of IGF-1 for neuroprotection after traumatic brain injury. Nanoscale 2022;14:18217-30.
79. Wilberger JE Jr., Harris M, Diamond DL. Acute subdural hematoma: Morbidity, mortality, and operative timing. J Neurosurg 1991;74:212-8.
80. Wilson L, Stewart W, Dams-O'Connor K, Diaz-Arrastia R, Horton L, Menon DK, *et al.* The chronic and evolving neurological consequences of traumatic brain injury. Lancet Neurol 2017;16:813-25.
81. Xiong Y, Mahmood A, Chopp M. Animal models of traumatic brain injury. Nat Rev Neurosci 2013;14:128-42.
82. Zweckberger K, Erös C, Zimmermann R, Kim SW, Engel D, Plesnila N. Effect of early and delayed decompressive craniectomy on secondary brain damage after controlled cortical impact in mice. J Neurotrauma 2006;23:1083-93.

How to cite this article: Buccilli B, Alan A, Aljeradat BG, Shahzad A, Almealawy YF, Chisvo NS, *et al.* Neuroprotection: Surgical approaches in traumatic brain injury. Surg Neurol Int. 2024;15:23. doi: 10.25259/SNI_774_2023